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Comparison of Local and Systemic Ibuprofen for Relief of Postoperative Pain in Symptomatic Teeth with Apical Periodontitis

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Background: One of the aims of endodontic treatment is to control preoperative and postoperative pain. The present study evaluated the effects of local and systemic ibuprofen on postoperative pain. It aimed to determine the most effective method for relieving postoperative pain due to chemomechanical preparation.

Material/Methods: Ninety patients with symptomatic apical periodontitis were randomly assigned to local ibuprofen, systemic ibuprofen, and control groups (n=30 each). Chemomechanical preparations were performed using a ProTaper Universal Ni-Ti rotary file under 2.5% sodium hypochlorite and 17% ethylenediaminetetraacetic acid irrigation. After the root canals were dried with sterile paper points, while Odontocide paste was applied into the root canals of the patients in the local ibuprofen group, calcium hydroxide paste was applied into the root canals of the patients in the systemic ibuprofen and control groups. Following completion of the endodontic treatment procedure, 200 mg ibuprofen was prescribed to patients in the systemic ibuprofen group. Friedman and Wilcoxon tests were used for statistical analysis.

Results: Posttreatment pain scores were recorded at 6, 12, 24, and 48 h using a visual analogue scale. Although there were no significant differences between the local ibuprofen group (Odontocide) and the control group (Ultracal) ($P>0.05$), pain scores in the systemic group (Ultracal+200 mg ibuprofen) were significantly lower than those in the other 2 groups ($P<0.05$).

Conclusions: These results indicate that systemic administration of ibuprofen is effective for postoperative pain relief.

Keywords: Ibuprofen • Pain, Postoperative • Periapical Periodontitis

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Background

Postoperative pain is an undesirable and common sensation for patients after endodontic procedures. The frequency of complications ranges from 3% to about 58% following root canal therapy [1]. Postoperative pain is usually due to an acute inflammatory response to chemomechanical preparation [2]. The causes of postoperative pain include chemical mediators, phenomena related to the immune system, cyclic nucleotide changes, psychological factors, and/or microbial injury to the periapical tissues [3].

The management of postoperative pain is challenging and involves the use of analgesics. Non-steroidal anti-inflammatory drugs (NSAIDs), acetaminophen, and opioids are typically prescribed for pain relief. The mechanism of action of most NSAIDs is inhibition of cyclooxygenase (COX) enzymes, which synthesize prostaglandins [4]. COX-1 is expressed constitutively and produces prostaglandins, which have protective effects in the gastrointestinal tract [5], whereas COX-2 is expressed in inflammatory cells [6]. Ibuprofen is a non-selective NSAID that inhibits both COX-1 and COX-2 [7] and is effective for alleviating dental pain [8-10].

The hypothesis of the present research was to investigate whether it would be more beneficial to use ibuprofen, an NSAID, locally or systemically, for the postoperative pain of endodontic patients. It is well known that controlling pain caused by bacterial infection is a clinical necessity. Therefore, calcium hydroxide needs to be used for bacterial reduction.

Bergenholtz and Spångberg reported that the microbiological goals of endodontic treatment of infected teeth were to reduce the number of microorganisms and prevent microbial recolonization of the treated canal [11]. Microorganisms can be eliminated from the root canal by mechanical debridement and irrigation with chemical solutions, but bacteria survive in the root canals of 40-60% of infected teeth after chemomechanical procedures [12-18]. Inter-session calcium hydroxide administration significantly increases the antibacterial activity [12,16,17,19].

Arruda et al compared a triple antibiotic paste (minocycline, metronidazole, and ciprofloxacin) and calcium hydroxide/chlorhexidine gluconate paste as intracanal medication materials in teeth with primary apical periodontitis [20].

Singh et al used 2% chlorhexidine gel and calcium hydroxide paste to assess postoperative pain relief efficacy in patients with acute apical periodontitis [21].

The aim of the current study was to compare the effectiveness of local (intracanal dressing) and systemic (oral) ibuprofen administration on postoperative pain following complete chemomechanical preparation. The present results are intended to guide endodontists in terms of whether to use ibuprofen in symptomatic apical periodontitis cases, and in cases when it will be used, to choose between local or systemic administration.

Material and Methods

This study was approved by the Ethics Committee of Batman University (2022/02-09). After informed consent was obtained, 90 adult patients with symptomatic (≥7 VAS score) apical periodontitis in mandibular premolar teeth diagnosed on the basis of their clinical and radiographic findings were included in the study and randomly assigned into 3 groups (each group containing 30 patients) in the study. The convenience sampling method was used to allocate the patients into the 3 different groups.

The inclusion criteria were root canal treatment for endodontic pain, not using analgesic drugs before endodontic treatment, a good health status (eg, no diabetes mellitus, neuralgia, cardiac disease, or active asthma), and provision of informed consent before the study began. The exclusion criteria were a history of allergy to local anaesthetics and NSAIDs, pregnant or nursing patients, antidepressant or anticoagulant use, and a history of endodontic treatment.

Endodontic Procedures

After administration of local infiltration anaesthesia (ULTRACAIN® D-S; Sanofi, Istanbul, Turkey), isolation was performed with a rubber dam, and an endodontic access cavity was produced. Pulp tissue was removed with #20 barbed broaches (Mani, Tokyo, Japan). A #15 K-file (DentsplyMaillefer, Ballaigues, Switzerland) was inserted to working length (WL), as determined by a Raypex 6 (RAY; VDW GmbH, Munich, Germany) electronic apex locator to establish patency before mechanical preparation. The WL was verified by periapical radiography. Root canals were undertaken using a ProTaper Universal (PTU; DentsplyMaillefer, Ballaigues, Switzerland) up to F2 file, under irrigation with (5 ml/min) 2.5% sodium hypochlorite (NaOCl), (5 ml/min) 17% ethylenediamine tetra-acetic acid (EDTA), (5 ml/min) 2.5% NaOCl, and (5 ml/min) saline. They were then dried using sterile paper points (PTU; DentsplyMaillefer, Ballaigues, Switzerland). The patients were randomly assigned (using convenience sampling) to Group 1 (local ibuprofen) Odontocide™ (Australian Dental Manufacturing, Brisbane, QLD, Australia), Group 2 (systemic ibuprofen) (Nurofen 200 mg; Abdi Ibrahim, Istanbul, Turkey), or Group 3 (control). Odontocide™ (a commercially prepared endodontic dressing that contains 20% calcium hydroxide and 7% ibuprofen) was used in the canal with lentulo spirals (Dentsply Maillefer) until the root canal was filled and condensed with hand pluggers in patients in the local ibuprofen group. In patients in the systemic

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Table 1. Pain levels.

Value	Pain level
0	Absolutely nothing
1	Very weak pain
2	Weak or light pain
3	Mild pain
4	Somewhat strong pain
5-6	Strong or heavy pain
7-9	Very strong pain
10	Extremely strong pain

ibuprofen group, calcium hydroxide paste (Ultracal XS, Ultradent, South Jordan, UT/Clinical Research Dental, Ontario, Canada) was applied to the canal in the same way, and each patient was prescribed 200 mg ibuprofen twice daily. In the control group, Ultracal was directly placed inside the canal. A sterile cotton pellet was placed in the access cavity, which was restored using temporary restorative material (Cavit G, 3M ESPE, GmbHCo, Seefeld, Germany). After 2-4 weeks, the root canals were filled using the cold lateral compaction method.

Patient Information

The numerical rating scale (NRS) was used to evaluate pain at 6, 12, 24, and 48 h after the endodontic procedure. The patients were contacted by telephone at predetermined time points post-procedure to remind them to complete and return the forms. The level of pain was rated according to **Table 1**. All of the patients were advised to contact the clinic or a researcher if their treatment protocol did not provide pain relief or if any other emergency occurred.

Statistical Analysis

Mean and Standard deviation (SD) for continuous variables, and median values for discrete variables, were calculated. The normality of the variables was analyzed with the Kolmogorov-Smirnov test. A 2-way Friedman test was used because the data did not show a normal distribution. The Wilcoxon test was applied for binary comparisons over time. Binary comparisons were also performed for the study groups (**Table 2**).

Two-sided *P* values were considered statistically significant at $P \leq 0.05$. Statistical analyses were carried out using R software/programming (version 3.6.2 (2019-12-12) – CRAN).

Sample Size

A previous study conducted on this same subject that investigated the effectiveness of rofecoxib in comparison with ibuprofen found that the pain was reduced by at least 50%, up to 24 hours after the start of the treatment [22]. In the present study, considering ibuprofen's expected rate of at least 70%, according to the R software, it was calculated that at least 82 patients should be recruited to attain 95% power.

Table 2. Patient and statistical variables.

	Local ibuprofen group	Systemic ibuprofen group	Control group
Number of patients	30	30	30
Male-to-Female ratio	14: 16	13: 17	13: 17
Median age	28	34	32
Pain minimum	0	0	0
Pain maximum	9	3	9
Pain mean 6 h	3.2333	0.3000	5.9333
Pain mean 12 h	3.0333	0.2333	5.6333
Pain mean 24 h	1.9333	0.2667	4.5333
Pain mean 48 h	1.3000	0.1000	3.4667
SD 6 h	2.67406	0.83666	2.13240
SD 12 h	3.31645	0.77358	1.88430
SD 24 h	2.40593	0.73968	2.12916
SD 48 h	1.98529	0.40258	2.50149

SD – standard deviation.

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Table 3. Statistical variables.

	6 h	12 h	24 h	48 h
Local/systemic ibuprofen groups	0.002	0.014	1.000	1.000
Local/control ibuprofen groups	0.232	0.079	0.036	0.219
Systemic/control ibuprofen groups	0.000	0.000	0.000	0.001

Results

Statistical Analysis Results for Local Ibuprofen, Systemic Ibuprofen, and Control Groups

Pain values were significantly lower in the systemic ibuprofen group than in the local ibuprofen group at 6 and 12 h ($P<0.05$).

At 24 and 48 h, pain scores were lower in the systemic ibuprofen group than in the local ibuprofen group, albeit not significantly different ($P>0.05$) (**Table 3**). At 6, 12, and 48 h, pain values were lower in the local ibuprofen group than in the control group, albeit not significantly different ($P>0.05$). At 24 h, the local ibuprofen group had a significantly lower pain score than the control group ($P<0.05$). At all of the time points, pain values were significantly lower in the systemic ibuprofen group ($P<0.05$).

Discussion

Pain is a relative feeling that is affected by physical and psychological factors; therefore, the objective evaluation of pain sensation is critical. Ibuprofen is effective for relieving pain after endodontic treatment [23,24], and is widely used to provide anaesthesia before treatment [25,26].

In the current study, postoperative pain relief after endodontic therapy provided by systemic and local administration of ibuprofen was evaluated. The patients in the systemic ibuprofen group had significantly lower pain values than those in the local ibuprofen and control groups. Significant differences were only found at 6 and 12 h, but pain values were lower in the systemic ibuprofen group than in the other 2 groups at all of the time points. In addition, pain scores at all of the time points were higher in the control group than in the other 2 groups.

When the median values obtained from the scores of the study groups were evaluated, it was determined that while the postoperative pain level was moderate in the first 12 hours in the local ibuprofen group, the postoperative pain remained at a low level in the 24th and 48th hours. In the systemic ibuprofen group, very low postoperative pain values were observed in all time periods starting from the 6th hour. In the control group, while there were severe postoperative pain values in the 6th and 12th hours, these values decreased slightly in the 24th hour, and then regressed to moderate pain values in the 48th hour.

Smith et al reviewed the efficacy of NSAIDs for postoperative endodontic pain, and reported that pain values peak at 6 to 12 h after anaesthesia [27]. We found that at 6 to 12 h, pain values were significantly lower in the systemic ibuprofen group than in the local ibuprofen group. The NRS, which had been used in previous studies [28,29], was selected for postoperative pain assessment in our study due to its ease of application and provision of detailed information. Whether ibuprofen inhibits COX 1 or COX 2 synthesis is unclear, but it is known to have activity in the central nervous system. In addition, the ibuprofen concentration must be greater than a minimum value to have a therapeutic effect [30].

Although there is no information in the literature regarding the effective blood concentration of ibuprofen when applied locally, due to the limit of vascularization at the root apex and the low concentration applied, we were not able to reach the minimum effective concentration; thus, the desired effects were not achieved.

Parirokh et al evaluated the efficacy of regular and as-needed ibuprofen in patients with irreversible pulpitis, and found no significant difference in pain relief up to 48 h. This may be due to the fact that the study involved patients with irreversible pulpitis without spontaneous pain and because their treatment was completed in a single session [24]. Rogers et al evaluated the effects of intracanal ketorolac, tromethamine, dexamethasone, and oral ibuprofen, on pain after endodontic treatment, and reported that there were no significant differences among the medications compared with placebo, although lower pain scores were obtained [31].

Calcium hydroxide absorbs the carbon dioxide generated by anaerobic bacteria in the canal [32], inactivates lipopolysaccharides in the outer membrane of Gram-negative bacteria [33], and facilitates tissue mineralization by stimulating fibronectin production [34]. Calcium hydroxide is frequently used in dentistry due to its antimicrobial and biological effects [35].

The NRS scores obtained for the evaluation of postoperative pain relief effectiveness in the study have some limitations, such as the subjective feeling of pain, the fact that pain intensity

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can be affected by daily emotional state, and the difficulty of scoring the sense of pain felt.

Hagenauer et al showed that pain sensitivity constitutes a daily pattern influenced by sleep state and circadian rhythm [36]. The fact that the endodontic treatment procedures in our study were performed at various times of the day may result in obtaining pain scores at different times of the day and may therefore provide data affected by different sleep states and circadian rhythms of the patients.

Conclusions

Despite the limitations of this study, according to our findings, systemic administration of ibuprofen appears to be a significantly more effective approach than local administration in reducing postoperative pain.

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